The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte
MOLLY F. KULESZ-MARTIN

Appeal No. 2001-1688
Application No. 08/811,361

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GRIMES, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claim 11, the only claim pending. Claim 11 reads as follows:

11. A purified peptide designated p53as peptide which peptide is present in p53as protein of a mammal and is identical to the unique carboxyl terminal region of p53as which distinguishes p53as protein from p53 protein, said peptide containing a unique epitope which is not present in p53.

The prior art relied upon by the examiner is:

Arai et al. "Immunologically Distinct p53 Molecules Generated by Alternative splicing". Molecular and Cellular Biology, Vol. 6 (September 1986), pp. 3232-3239.

Claim 11 stands rejected under 35 U.S.C. § 112, first paragraph (enablement).

Claim 11 stands rejected under 35 U.S.C. § 112, second paragraph, as indefinite.

Claim 11 stands rejected under 35 U.S.C. § 102(b) as anticipated by Arai.

We reverse and enter new grounds of rejection under the provisions of 37 CFR § 1.196(b).

Background

The p53 gene encodes a protein which binds to cellular factors and controls cell growth. The p53 gene is defective in over half of human cancers. Introduction of a normal p53 gene into a variety of cancer cells arrests their growth. Replacement of a single amino acid can be sufficient to change the normal folding of the p53 protein making it inactive as a growth control gene. See, generally, specification page 1. The carboxy terminus of p53 contains a domain that can turn off its regulatory function. In other words, an "always active" p53 is made by truncating the carboxy terminus (reply brief, pages 1-2). Prior to the effective filing date of the present application, it was known that alternatively spliced p53 RNAs existed in normal cells and tissues and in tumor cells (specification, page 2). The present invention involves the protein encoded by the alternatively spliced p53 mRNA and particularly involves the carboxy-terminal

sequences which differ between the proteins encoded by the conventionally-spliced and alternatively-spliced p53 mRNAs (e.g., specification pages 9 and 10).

Discussion

Claim construction

We begin with an analysis of claim construction as this is central to the issues on appeal. First, the claim recites "A purified peptide designated p53as peptide" and "p53as protein." We note that the specification does not contain an explicit definition of the metes and bounds of "peptide" and "protein." However, "the definiteness of the language employed [in a claim] must be analyzed--not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971)(footnote omitted). Although the biochemistry art does not recognize a bright line between "peptide" and "protein," the term "peptide" is often used in the art to refer to a low molecular weight material.[1] The specification consistently uses the term "p53as protein" when referring to a full size product encoded by an mRNA, and consistently uses the term "p53as peptide" when referring to a smaller portion of a protein, e.g., a 17-amino acid peptide

[1]Peptide: Biochemistry. Any member of a class of compounds of low molecular weight that yield two or more amino acids on hydrolysis, and that form the constituent parts of proteins. Academic Press Dictionary of Science and Technology

obtained from a mouse protein sequence (see specification page 12) or a 20 amino acid peptide obtained from a human sequence (see specification page 25). Therefore, for the purposes of this case, a "p53as peptide" nomenclature adopted by the appellant is interpreted as meaning a product smaller than a "p53as protein."

Second, we must determine the meaning and scope of "p53as." On pages 2 and 3 of the specification it is stated that the protein designated p53as "is present in normal cells of a mammal and is essentially identical to known normal growth controlling protein p53 of the same mammal, at least until the final 50 amino acids of the carboxy terminal end of the protein. .... The final 50 amino acids of p53as protein...are at least partly different than the final 50 amino acids of p53 protein. ... It is believed that the most common and probable final few amino acids at the carboxy termination of p53as contain the sequences SPNC and SPPC." On page 9, the specification states "...the inventor has now discovered a novel form of a wild type (normal) p53 protein and demonstrated that it is present in nontransformed mouse cell strains and mouse squamous cell carcinomas. Designated p53as, (alternatively spliced p53) it arises from a normal variation in processing of the p53 messenger RNA (mRNA)." Therefore, we understand "p53as" as referring to a protein encoded by a messenger RNA found in nontransformed normal cells; the mRNA being the product of alternative splicing of the p53 gene transcript, and the encoded protein differs from p53 within the carboxy-terminal 50 amino acids. The peptide of the claim "is identical to the

unique carboxy terminal region of p53as which distinguishes p53as protein from p53 protein, said peptide containing a unique epitope which is not present in p53."

In conclusion, we construe the claim as being drawn to a peptide which is identical to the unique sequence which differentiates the carboxy terminal regions of p53 protein and the "p53as protein" encoded by alternatively spliced p53 mRNA in normal mammalian cells. The peptide furthermore contains an epitope present in p53as but not present in p53.

35 U.S.C. § 112, first and second paragraphs

One is not in position to determine whether a claim is enabled under the first paragraph of 35 U.S.C. § 112 until the metes and bounds of that claim are determined under the second paragraph of this section of the statute.[2] Therefore, we treat this issue first.

The examiner's position is that the claim is indefinite because "p53as" is a laboratory designated term which the art does not recognize to be unique and unambiguous and because the metes and bounds are not known for a peptide "identical to the unique carboxyl terminal region which distinguishes p53as from p53 protein." However, analyzing the claim in light of the disclosure, we find that the

[2] In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971).

specification provides an understandable definition of "p53as" and an understandable definition of the "unique carboxy terminal region...." The claim is broad in that it reads upon peptides encoded by alternatively spliced p53 mRNA from any species of mammal. However, breadth is not indefiniteness. In re Gardner, 427 F.2d 786, 787, 166 USPQ 138, 141 (CCPA 1970). Therefore we do not sustain this rejection.

The rejection under 35 U.S.C. § 112, second paragraph, is reversed.

The examiner's position on enablement is that the specification does not enable a person skilled in the art to make the invention commensurate in scope with the claim. The examiner states that the specification identifies two unique peptide sequences "as part of p53as," namely SEQ ID Nos. 1 and 2 but does not teach other species. The examiner states that it is unpredictable whether other forms of p53 can be identified and cloned using the same primers and strategies and that the specification does not provide any guidance as to how to produce peptides specific to p53as which could encompass deletions, mutations, substitutions in the sequence.

However, we note that the specification provides guidance to the source of alternatively spliced p53 mRNA (in normal cells, page 2), and teaches alternative splicing in intron 10 in human and mouse species (pages 9, 21). While some experimentation would be required to determine the structure of p53 and p53as for the full scope of mammals, and to prepare a peptide which is (a) identical to the unique carboxy terminal region of p53as for some mammal and (b) possesses a unique epitope which is not present in p53 of that mammal, the examiner has not adequately

established that such experimentation would be undue. Absent a fact-based explanation from the examiner as to why the needed experimentation would be undue, we find that the examiner has not established a prima facie case of non-enablement.

The enablement rejection is reversed.

Anticipation

The claim stands rejected as anticipated by Arai. In making this rejection, the examiner interprets the phrase "which peptide is present in p53as protein" as meaning that the peptide is contained within the p53as protein and concludes that the claim reads upon the p53as protein per se as disclosed in Arai. As discussed above, we construe the claim differently and as result, do not agree with the examiner's position that the claimed p53as peptide reads upon the full-size p53as protein.

The anticipation rejection is reversed.

New Grounds of Rejection

Under the provisions of 37 CFR § 1.196(b), we make the following new ground of rejection.

Claim 11 is rejected under 35 U.S.C. § 112, first paragraph (written description).

Whether a specification complies with the written description requirement of Section 112, Para. 1, is a question of fact[3]. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of

[3] Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); Ralston Purina Co. v. Far-Mar Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985).

biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. at 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

Although the analysis in Lilly was directed to inventions involving DNA and the present claim is directed to peptides, we find that Lilly is applicable here. The basic rationale of the Lilly decision is that the criteria for assessing the written description of chemical compounds applies to all chemical compounds, even compounds as complex as DNA. See Lilly, 119 F.3d at 1567, 43 USPQ2d at 1405:

> [a] description of rat insulin cDNA is not a description of the broad classes of vertebrate or mammalian insulin cDNA. A written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials.

Therefore, the Lilly holding applies to proteins and peptides such as those claimed here. A specification may provide an adequate description of the genus of the claim by structurally describing a representative number of species within the genus or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." We do not find either situation is present here.

Claim 11 is drawn to a genus of peptides, defined by reference to two named proteins (p53 and p53as) encoded by alternatively spliced mRNAs. The claim does not define the relevant peptide in structural terms.

The present specification describes the structure (amino acid sequence) of p53as peptides from two mammalian species, mouse and human, and also states that "it is believed that the most common and probable final few amino acids at the carboxy

termination of p53as contain the sequences SPNC and SPPC." The specification does not, however, attempt to describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Therefore, the issue under Lilly is whether the present specification's description of two p53as peptides and two "most common and probable" terminal tetramer sequences is representative of the claimed genus. The claimed genus encompasses p53as peptide from any mammal, i.e., any primate, rodent, ruminant, cetacean, feline, canine, etc. The specification itself shows that p53as peptides vary considerably in that there is no striking similarity between SEQ ID:1, the mouse peptide LQPRAFQALIKEESPNC, and SEQ ID:4, the human peptide REKGHRPSHSCDVISPPCFC. The skilled artisan would reasonably expect a similar degree of variability between other groups of mammals that are not closely related, for example, primates and ruminants.

The specification does not attempt to describe structural features that are common to all p53as peptides. Therefore, the description provided by the specification does not allow a skilled artisan to "visualize or recognize the identity of the members of the genus." Thus, the specification does not adequately describe the genus recited in the claim.

Other Issues

We point out the following for consideration should this case undergo further prosecution. The examiner's attention is directed to Han et al, "Alternatively spliced p53 RNA in transformed and normal cells of different tissue types," Nucleic Acids Research, Vol. 20, p. 1979-1981, April 25, 1992. The reference teaches that sequence of the 3' ends of the alternatively spliced p53 nucleic acids are identical to those taught by Arai. See the passage spanning pages 1980 and 1981. Han also points out on page 1981 that a p53 protein coded by the alternatively spliced RNA would differ from the regular p53 protein by 25 amino acids at the C-terminus, notes that the C-terminal sequences are "quite distinct," notes that the differences "could lead to significant biochemical and biological changes," and states that "more precise biochemical and biological characterization of AS-p53 protein along with R-p53 protein appear to be critical in future studies of p53 function in normal cells and in oncogenesis." Han also states that "Future studies of a distinct AS-p53 protein and its biological significance will be facilitated by specific antibody to AS-p53 protein." The question arises as to whether the explicitly stated desire to obtain specific antibody to AS-p53 protein and the discussion of distinctive structures of the C-terminal 25 amino acids which distinguish the AS protein from the regular protein would have reasonably suggested to one of ordinary skill a purified peptide reproducing the distinctive C-terminal 25-amino acid sequence to be used for inducing the desired specific antibody? If so, claim 11 may be

unpatentable. The fact finding and analysis needed in order to resolve this question is best performed by the examiner in the first instance.

Time Period for Response

This opinion contains a new ground of rejection pursuant to 37 CFR § 1.196(b). 37 CFR § 1.196(b) provides that, "A new ground of rejection shall not be considered final for purposes of judicial review."

37 CFR § 1.196(b) also provides that appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (§ 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .
>
> (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED; 37 CFR § 1.196(b)

Sherman D. Winters)
Administrative Patent Judge)
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)
William F. Smith) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
)
Eric Grimes) INTERFERENCES
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Appeal No. 2001-1688
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